## REMARKS

Claims 34-42 and 64 are pending upon entry of this amendment. Claim 38 has been amended to further specify the region of complementarity. Support is found in the specification at least at page 9, paragraph 43. No new matter has been introduced by the amendments.

### I. Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 38, 40, and 42 are rejected as allegedly indefinite. The rejection is respectfully traversed.

**A. Alleged Indefiniteness of "operably associated"**

The term "operably associated" in claims 40 and 42 is said to be vague and indefinite. Applicants respectfully disagree.

The Examiner states in Paper No. 9 at page 2 that the disclosure pointed to in Applicants' previous response supports a series of nucleotides being operably linked. However, the Examiner maintains that the cited disclosure "does not support that the specification discloses nucleotides being operably associated as stated in claims 40 and 42." *See* Paper No. 9 at page 2, paragraph number 6. The Examiner states that

> The phrase 'operably associated' is vague and indefinite because it is unclear what criteria are bing used to consider polynucleotides as being 'operably associated' (i.e. being adjacent via phosphodiester bonds or binding nucleotide sequence via thermal dynamic forces). Applicants can resolve this issue by particularly pointing out the criteria that is being used to determine polynucleotides are 'operably associated.' Clarification of the metes and bounds of the instant claims is required.

Paper No. 9 at page 3, paragraph No. 7.

Applicants respectfully submit that the issue of whether the specification supports nucleotides being operably associated as stated in claims 40 and 42 is an issue of written description, which is dealt with below. With respect to the metes and bounds of the instant claims, the examples of operable association disclosed in the specification involve regulatory sequences present in the same nucleic acid molecule, *i.e.*, attached by covalent linkage, as the disclosed fragment of an E. coli pathogenicity island.

Applicants submit that the metes and bounds of the instant claims are clear and definite, and the rejection should be reconsidered and withdrawn.

**B. Alleged Indefiniteness of "sequence complementary"**

The use of "sequence complementary" in claim 38 is said to be unclear with respect to the criteria used to determine that a sequence is complementary. The Examiner appears to find uncertainty in the length of the region of complementarity required in order for a complementary sequence to fall within the instant claims. In their previous response, Applicants amended claim 38 to recite "[a] nucleic acid sequence complementary to the entirety of the nucleotide sequence of claim 34." However, the Examiner states in Paper No. 9:

> It is acknowleged that Applicants have further limited the sequence of claim 34 to the entirety of the nucleotide sequence, however, such limitation does not resolve the issue of the term 'complementary' being vague and indefinite. The issue remains that it is unclear what criteria are being used to consider the claimed nucleic acid sequence to be complementary to the ntirety of the nucleotide of sequence of claim 34. Further, it is noted that claim 34 from which claim 38 depends, limits SEQ ID:65 to nucleotides 2889-1915. Clarification of the metes and bounds of the instant claims is required. It is suggested that Applicants could resolve the above vague and indefinite issue by amending claim 38 to include the phrase 'fully complementary.'

Paper No. 9 at page 3, paragraph No. 8. While not admitting that claim 38 in its previous form was in any way vague or indefinite, Applicants have amended claim 38 as suggested by the Examiner. Therefore, withdrawal of the rejection is respectfully requested.

## II. Claim Rejections under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 35, 36, 40, and 42 are rejected as allegedly containing new matter and therefore lacking written description. The rejection is respectfully traversed.

**A. Claims 35 and 36**

Claims 35 and 36 recite the phrase "heterologous polynucleotide sequence," which the Examiner considers to be new matter. Applicants respectfully disagree.

Applicants' previous response argued that the phrase "heterologous polynucleotide sequence" does not require definition in the specification because it is merely a term of art which is used with its ordinary meaning. However, the Examiner maintains the issue is not the meaning of the phrase, but that "the limitation was not disclosed as filed."

The specification clearly discloses that polynucleotides of the invention can include a heterologous polynucleotide sequence, which may encode a polypeptide, as recited in claims 35 and 36. For example, the specification describes recombinant constructs and vectors comprising one or more of the disclosed fragments of *E. coli* pathogenicity islands:

> The present invention further provides recombinant constructs comprising one or more fragments of the *E. coli* J96 PAIs. The recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into which, for example, an *E. coli* J96 PAI ORF is inserted. The vector may further comprise regulatory sequences, including for example, a promoter, operably linked to the ORF.

Specification at paragraph [0068]. Clearly, the recombinant constructs, vectors, plasmids, viral vectors, regulatory sequences, and promoters described in the above passage exemplify several types of "heterologous polynucleotide sequence" of the type recited in claim 35. Furthermore, the specification teaches the inclusion of polynucleotide sequences which encode polypeptides, as recited in claim 36. Such polypeptides are exemplified by chimeric proteins and fusion proteins:

> As one of skill in the art will appreciate, *E. coli* PAI polypeptides of the present invention and the epitope-bearing fragments thereof described above can be combined with parts of the constant domain of immunoglobulins (IgG), resulting in chimeric polypeptides. These fusion proteins facilitate purification and show an increased half-life *in vivo*. This has been shown, e.g., for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins (EP A 394,827; Traunecker *et al., Nature 331*:84- 86 (1988)). Fusion proteins that have a disulfide-linked dimeric structure due to the IgG part can also be more efficient in binding and neutralizing other molecules than the monomeric *E. coli* J96 PAI proteins or protein fragments alone (Fountoulakis *et al., J. Biochem 270*:3958-3964 (1995)).

Specifiation at paragraph [0097]. A further example is the use of epitope-bearing polypeptides of the invention fused to a carrier protein:

> The epitope-bearing peptides and polypeptides of the invention may be produced by any conventional means for making peptides or polypeptides including recombinant means using nucleic acid molecules of the invention. For instance, a short epitope-bearing amino acid sequence may be fused to a larger polypeptide, which acts as a carrier during recombinant production and purification, as well as during immunization to produce anti-peptide antibodies.

Specification at paragraph [0092]. Thus, claims 35 and 36 do not introduce new matter with respect to the use of "heterologous polynucleotide sequence," and withdrawal of the rejection is respectfully requested.

**B. Claims 40 and 42**

The recitation of "polynucleotide is operably associated" in claims 40 and 42 is also said to introduce new matter. Applicants respectfully disagree.

The Examiner acknowledges that the passage cited in Applicants' previous response supports that operable linkage or association has written description. However, the Examiner maintains that the previously recited passage "does not support that the specification discloses the operable association of a 'heterologous' regulatory sequence, which is considered to be new matter." Paper No. 9 at page 4, paragraph No. 13.

The specification clearly teaches the use of heterologous regulatory sequences in operable association with the disclosed polynucleotides. For example,

> Large numbers of suitable vectors and promoters are known to those of skill in the art and are commercially available for generating the recombinant constructs of the present invention. The following vectors are provided by way of example. Bacterial: pBs, phagescript, PsiX174, pBluescript SK, pBs KS, pNH8a, pNH16a, pNH18a, pNH46a (Stratagene); pTrc99A, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia). Eukaryotic: pWLneo, pSV2cat, pOG44, pXT1, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia).
> Promoter regions can be selected from any desired gene using CAT (chloramphenicol transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda $P_R$, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art.

Specification at paragraphs [0068] and [0069]. Thus, it is respectfully submitted that the term "polynucleotide is operably associated" does not introduce new matter, and withdrawal of the rejection is requested.

## III. Claim Rejections under 35 U.S.C. § 102(e)

Claim 38 is rejected as allegedly anticipated by Valenuela et al., U.S. Patent 5,814,478. The rejection is respectfully traversed.

The Examiner has presented an alignment showing that portion of SEQ ID NO:31

of Valenuela et al. is complementary to nucleotides 2459-2465 of SEQ ID NO:65 of the instant case. Thus, according to the Examiner, Valenuela et al. disclose a nucleic acid sequence which is complementary over only seven contiguous nucleotides to ORF ID 4 of CONTIG ID 65. However, claim 38 recites a nucleic acid sequence fully complementary to the entirety of the nucleotide sequence of claim 34. Because Valenuela et al. disclose only seven contiguous nucleotides of the complement of ORF ID 4 of CONTIG ID 65, Valenuela et al. do not anticipate claim 38. Therefore, withdrawal of this rejection is respectfully requested.

## CONCLUSION

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. Applicants believe that this application is now in condition for allowance.

If there are any fees due in connection with the filing of this paper, please charge the fees to Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to Deposit Account No. 08-3425.

Respectfully submitted,

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